## REMARKS

In the present amendment, claim 43 is canceled without prejudice or disclaimer, and claims 25, 26, 32 and 33 have been amended. As a result of this amendment, claims 25, 26, 32, 33, 39-41 and 44-46 are pending in the application, with claims 45-46 currently withdrawn from consideration. It is believed that this Amendment is fully responsive to the Office Action dated May 9, 2005.

Applicant submits that no new matter is added by this amendment. Support for the amendments to the claims is discussed below.

**The rejection of claims 25-26, 32-33, 39-41 and 43-44 under 35 U.S.C. §103(a) as being unpatentable over Saito et al., (WO 94/23019) and Yoshida et al., (Virology 1994 Vol. 200) and further in view of Nazerian et al. (EP 520,753) is maintained for reasons already of record.** (Office Action paragraph no. 3)

The rejection is overcome by the amendments to base claims 25, 26, 32 and 33. The claims have been amended with the clarifying clause: "there being no existence of a membrane anchor peptide". Support for this clarifying amendment may be found in claim 43 (now canceled), and in the specification of the application at page 8, lines 15-16, where the specification states that: "the polypeptides may contain only a signal sequence for that purpose." Support may also be found in Examples 1 and 2 specification (pages 16-19), wherein the plasmids pNZ4OK-S and pNZ40K-C were constructed having no membrane anchor peptide. Claim 43 has accordingly been canceled to avoid redundancy.

In the present claims, the invention is a recombinant Avipox virus or vaccine containing the DNA encoding the fusion protein wherein a signal polypeptide of herpes virus glycoprotein B protein (gB signal polypeptide) is ligated with an antigenic protein isolated from Mycoplasma gallisepticum (MG antigenic protein) at the N-terminus thereof, and there is no existence of a membrane anchor peptide.

That is, the claimed invention is characterized by a fusion protein wherein **the gB signal polypeptide is ligated with the MG antigenic protein at the N-terminus thereof, and there is no existence of a membrane anchor peptide**. This structural feature of the present invention enables the MG antigenic protein expressed in host cells to be secreted extracellularly. As a result, the recombinant Avipox virus or vaccine containing the DNA encoding the fusion protein having the above characteristics is extremely effective in *in vivo* vaccination.

In this regard, Examples 1 to 3 of the present specification show the actual construction of the recombinant fowl pox viruses (EPV) 40K-C and 40K-S.

The virus 40K-S contains a DNA encoding a fusion protein having the gB signal polypeptide of Marek's disease virus ligated with the MG antigenic protein (TTM-1) at the N-terminus thereof and having no membrane anchor peptide.

The virus 40K-C contains a DNA encoding a fusion protein having the gB signal polypeptide of Marek's disease virus ligated with the MG antigenic protein (TTM-1) at the N-terminus thereof, through the gB antigenic protein of Marek's disease virus (GB antigenic protein), and having no membrane anchor peptide.

The structures of the viruses 40K-C and 40C-S are schematically shown in Annex I attached hereto. As seen from Annex 1, the MG antigenic protein or the MG antigenic protein fused with the GB antigenic protein **can be secreted extracellularly due to the gB signal polypeptide and due to no existence of a membrane anchor peptide.**

Further, Example 5 of the specification of the application demonstrates that the recombinant viruses 40K-C and 40K-S induced highly effectively antibodies against Mycoplasma gallisepticum. Moreover, Example 6 demonstrates the highly effective *in vivo* vaccination of the 40K-C and 40K-S viruses.

The results of Example 6 are summarized in Table A, below. Table A shows also the results of the prior art virus of Saito as compared with those of the viruses 40K-C and 40K-S of the present invention, as discussed in more detail below.

Table A summarizes the results of Table 3 of Example 6 of the present specification, and those of the Rule 132 Declaration of Mr. Shuji Saitoh that was submitted to the U.S. Patent and Trademark Office on June 27, 2000. The results of the recombinant viruses of Saito were obtained by conducting the same challenge test as described in Example 6 on Saito's recombinant viruses.

**TABLE A**

| | Recombinant virus | Structure | Lesion Score Average | ±SE |
|---|---|---|---|---|
| Saito | fNZ2929XM1 | NH final-HN membrane anchor-MG 40K gene | 2.46 | 0.21 |
| | fNZ7929-67 | MG 67K gene | 2.02 | 0.20 |
| | fNZ7929-66 | MG 66K gene | 2.41 | 0.17 |
| Present invention | 40K-S | gB signal-MG 40K gene | 1.38* | 0.21 |
| | 40K-C | gB signal -GB antigenic protein gene - MG 40K gene | 1.89* | 0.16 |
| Challenge control | None | | 2.27 | 0.13 |

* Difference is SIGNIFICANT ($p<0.05$) compared to challenge control.

Comparison of the Present Invention with the Cited References

A. Saito et al. (WO 94/23019) ("Saito")

1) Saito describes a recombinant virus containing a DNA encoding a fusion protein wherein a signal polypeptide of HN gene of New Castle disease virus (NDV) is ligated with an antigenic protein of Mycoplasma gallisepticum (MG antigenic protein), through a membrane anchor peptide of HN gene of NDV.

For reference, the structure of the recombinant virus of Saito is schematically shown in Annex II attached hereto.

As seen from Annex II, although the MG antigenic protein is anchored to the host cell membrane and exposed extracellularly, **the MG antigenic protein cannot be secreted extracellularly due to the existence of the membrane anchor peptide.**

Therefore, **the recombinant virus of Saito containing the membrane anchor peptide gene is clearly different in the structure from the claimed virus of the present invention containing no membrane anchor peptide gene.**

2) Annex II, attached hereto, shows the results of Saito as compared with those for the viruses 40K-C and 40K-S of the present invention.

Table A, above, summarizes, together with the results of Table 3 of Example 6 of the specification of the present application, the results of the Rule 132 Declaration of Mr. Shuji Saitoh that was submitted to the U.S. Patent and Trademark Office on June 27, 2000.

As shown in Table A, chicken inoculated with the recombinant virus of Saito (i.e., fNZ7929-67, fNZ7929-66 and fNZ2929XM1) merely exhibited approximately the same average lesion score as non-inoculated chicken *in vivo* of the control.

Therefore, the results confirm that the recombinant virus of Saito is not effective in *in vivo* actual vaccination against Mycoplasma infection.

The fNZ2929SM1 has no membrane anchor peptide gene. The recombinant viruses

fNZ7929-67 and fNZ7929-66 have neither the signal polypeptide gene nor the membrane anchor peptide gene. Thus, those viruses are different in the structure from the claimed virus of the present invention.

On the other hand, the results shown in Table A indicate that the claimed recombinant Avipox virus or vaccine of the present invention is unexpectedly much more effective in *in vivo* vaccination than the recombinant viruses of Saito.

B. Nazerian et al. (EP 520753 A1) ("Nazerian")

Nazerian describes a recombinant fowlpox virus (FPV) expressing a full length of a glycoprotein B (gB) antigenic protein gene derived from Marek's disease virus. For reference, the structure of the recombinant FPB is schematically shown on Annex II.

As seen in Annex II, the recombinant FVD contains the gB antigenic protein gene flanked by the gB signal sequence at the C-terminus thereof and by the gB membrane anchor peptide sequence at the N-terminus thereof.

Therefore, although the expressed gB antigenic protein is anchored to the host cells, **the gB antigenic protein cannot be secreted extracellularly due to the existence of the membrane anchor peptide**.

Thus, **the recombinant virus of Nazerian containing the membrane anchor peptide gene is clearly different in structure from the claimed virus of the present invention containing no membrane anchor peptide gene**.

C. Yoshida et al. (Virology 1994 Vol. 200) ("Yoshida")

Yoshida describes an analysis on the GB protein gene derived from Marek's disease virus and an observation on the expression and membrane transmittance of the gB protein genes. Yoshida describes the extracellular exposure of the expressed gB protein gene after expression in the host cells. Therefore, the teaching of Yoshida is similar to that of Nazerian, discussed above.

To summarize, **the virus of Yoshida contains the membrane anchor peptide gene, and therefore is clearly different in the structure from the claimed virus of the present invention containing no membrane anchor peptide gene**.

D. Unexpected Results of the Present Invention

1) As discussed in detail above, clearly, **there are significant structural differences between the claimed virus and the prior art viruses**. In particular, the claimed virus has no membrane anchor peptide gene, whereas each of the viruses described in the cited references has a membrane anchor peptide gene.

2) All of the cited references teach virus containing the membrane anchor peptide gene. Consequently, **all of the references have no teaching of the influence of having "no existence of a membrane anchor peptide gene" on the actual *in vivo* effectiveness of vaccination**.

Thus, one of skill in the art at the filing date of the present application would have concluded that **a recombinant virus containing a membrane anchor peptide gene is effective in vaccination**.

Applicant further calls attention to Yanagida et al., U.S. Patent No. 5,286,639, which is made of record in the concurrently filed Information Disclosure Statement. Yanagida et al. describes that a recombinant Avipoxvirus containing a signal polypeptide gene, a membrane anchor peptide gene and HN gene of New Castle disease virus (NDV) was actually effective in the *in vivo* vaccination.

Unlike the prior art, the claimed recombinant virus of the present invention **is extremely effective** in *in vivo* vaccination **by having no membrane anchor peptide gene**.

Therefore, Applicant submits that the effectiveness of the claimed virus in *in vivo* vaccination is **unexpected** over the prior art**, and that the claimed invention therefore exhibits unexpected effects**.

Furthermore, in the cited references, there is no suggestion, motivation or teaching to combine the references to produce the claimed invention. As discussed in detail herein above, none of the cited references describes or suggests "no existence of a membrane anchor peptide gene in the recombinant virus". Applicant submits that there is no suggestion, motivation or teaching in the cited references to combine the references to produce the claimed invention.

Accordingly, pending claims 25-26, 32-33, 39-41 and-44 are not obvious over Saito et al., (WO 94/23019), Yoshida et al., (Virology 1994 Vol. 200) and Nazerian et al. (EP 520,753), taken separately or in combination.

**Claims 25-26, 32-33, 41 and 43-44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter**

**which applicant regards as the invention. Acronyms like gB must be spelled out when used for the first time in a chain of claims.** (Office Action paragraph no. 4)

The Office Action states that acronyms like "gB" must be "spelled out when used for the first time in a chain of claims". The rejection is overcome by the amendments to claims 25, 26, 32 and 33, in which "gB" is spelled out as –glycoprotein B–. Applicant submits that it is well known in the art that "gB" is an abbreviation for "glcyoprotein B".

In view of the aforementioned amendments and accompanying remarks, the claims, as amended, are believed to be patentable and in condition for allowance, which action, at an early date, is requested.

If, for any reason, it is felt that this application is not now in condition for allowance, the Examiner is requested to contact Applicant's undersigned agent at the telephone number indicated below to arrange for an interview to expedite the disposition of this case.

In the event that this paper is not timely filed, Applicant respectfully petitions for an appropriate extension of time. Please charge any fees for such an extension of time and any other fees which may be due with respect to this paper, to Deposit Account No. 01-2340.

Respectfully submitted,

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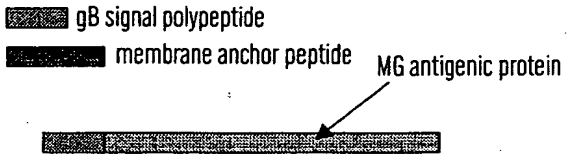
Enclosures: ANNEX I and ANNEX II

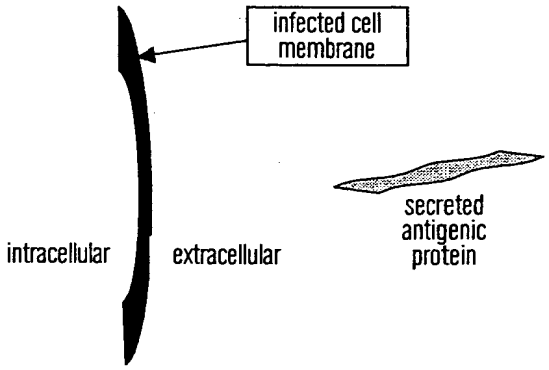
Q:\FLOATERS\DAG\DAG\98\981167\Amendment Accompanying RCE

# ANNEX I

## 40K-S

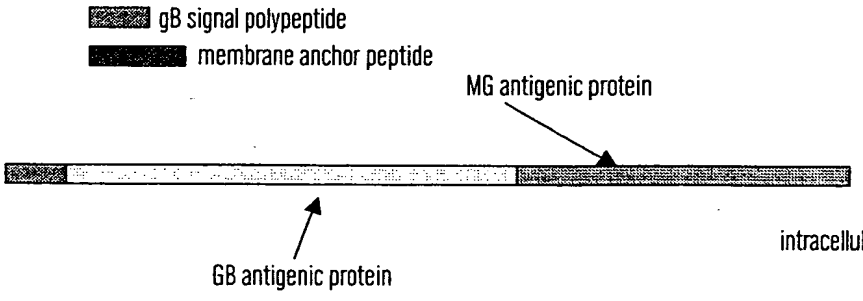



Structure of Recombinant Virus




Situations after Expression

## 40K-C

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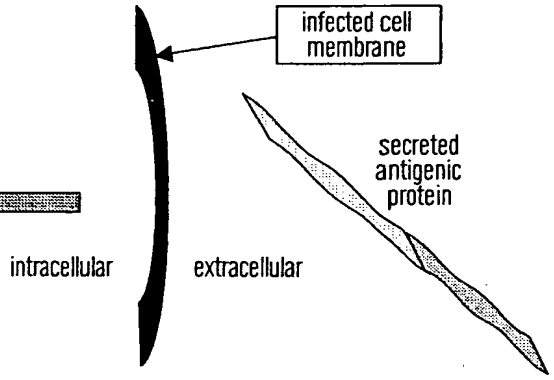
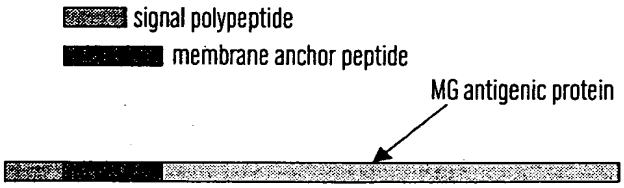



Situations after Expression

# ANNEX II

## Saito

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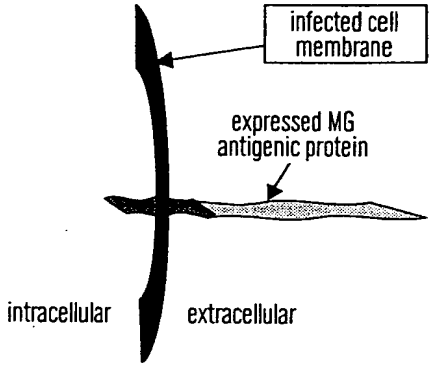
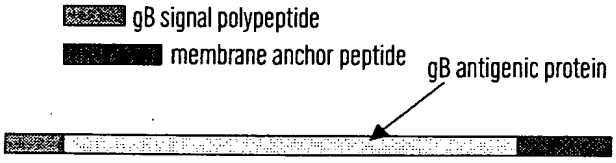
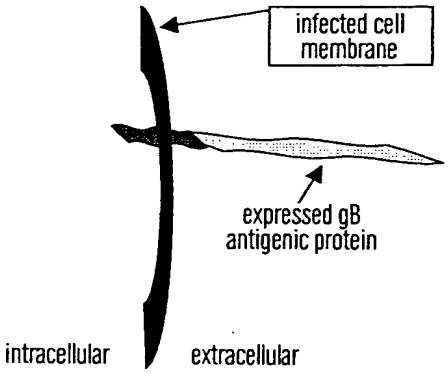



Situations after Expression

## Nazerian




Structure of Recombinant Virus




Situations after Expression